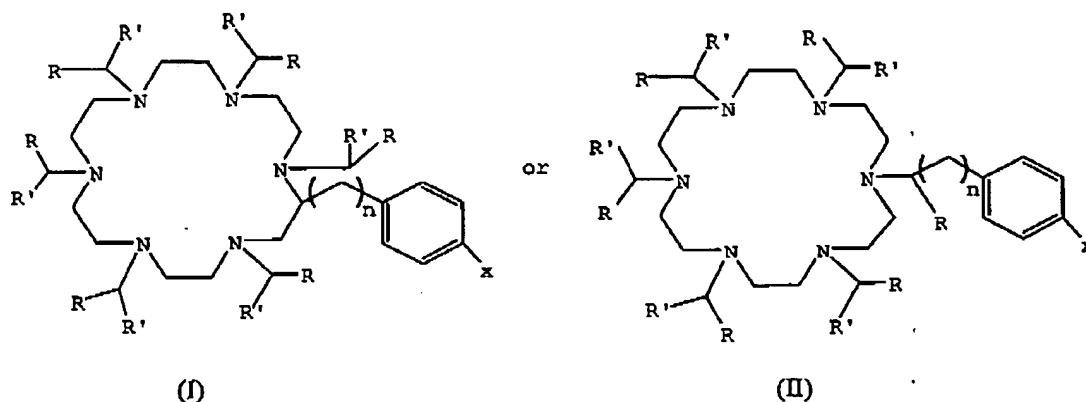


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CLAIM AMENDMENTS

1. (Original) A bifunctional compound of one of the following formulae:



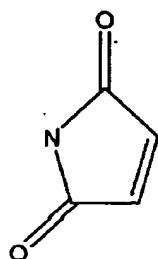
wherein for compound (I), R is selected from the group consisting of $P(O)R'OH$ and $P(O)(OR')OH$,

wherein for compound (II), R is selected from the group consisting of CO_2H , CONHR' , $\text{P}(\text{O})\text{R}'\text{OH}$ and $\text{P}(\text{O})(\text{OR}')\text{OH}$,

R' is selected from the group consisting of H, a C₁-C₈ alkyl, phenyl and benzyl, wherein said phenyl or benzyl is substituted or unsubstituted,

n is 1-6, and

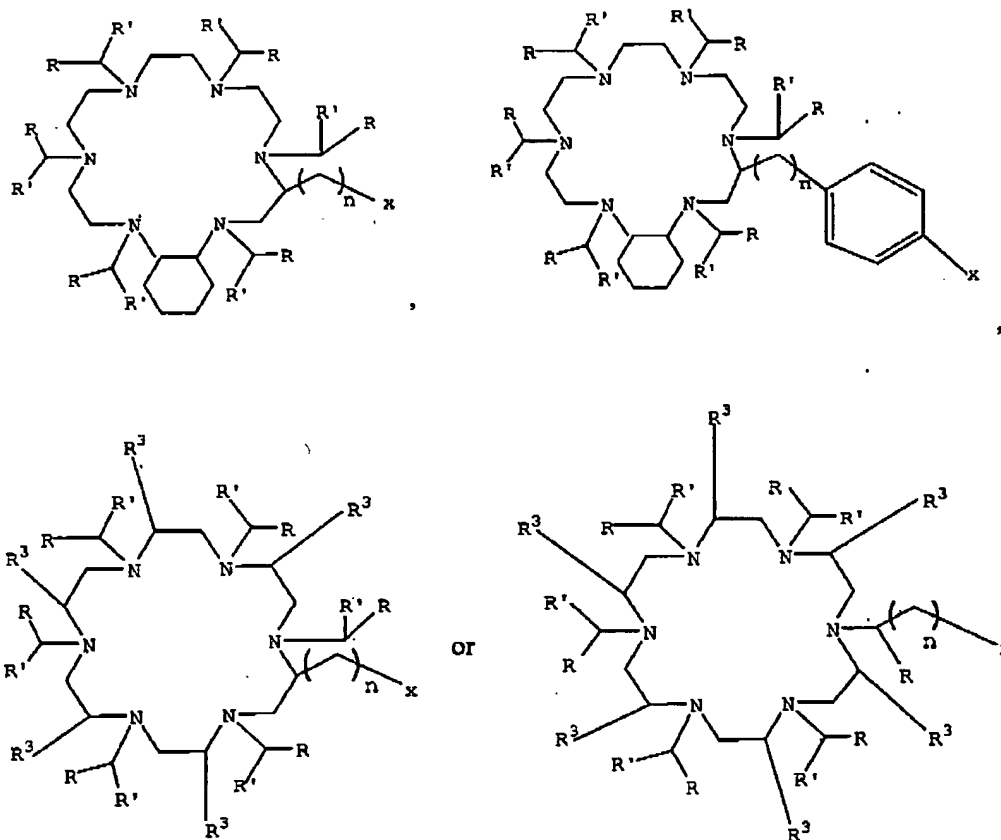
X is selected from the group consisting of NO₂, NH₂, NCS, NHC(O)CH₂Z, in which Z is selected from the group consisting of Cl, Br and I, and



wherein said compound is chelated to ^{225}Ac .

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2. (Original) A bifunctional compound of one of the following formulae:



wherein R is selected from the group consisting of CO₂H, CONHR', P(O)R'OH and P(O)(OR')OH,

R' is selected from the group consisting of H, a C₁-C₈ alkyl, phenyl and benzyl, wherein said phenyl or benzyl is substituted or unsubstituted,

n is 1-6, and

X is selected from the group consisting of NO₂, NH₂, NCS, NHC(O)CH₂Z, in which Z is selected from the group consisting of Cl, Br and I, and

R³ is selected from the group consisting of H, a C₁-C₆ alkyl, and benzyl, wherein said compound is chelated to ²²⁵Ac.

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3. (Currently Amended) The bifunctional compound of claim 1, wherein R is CO₂H and R' is H or CH₃ for compound (II).

4. (Original) The bifunctional compound of claim 1, wherein, when R' is phenyl or benzyl, said phenyl or benzyl can be substituted with one or more substituents selected from the group consisting of a C₁-C₆ alkyl, a halogen, a C₁-C₆ alkoxy, a C₁-C₆ hydroxyl, and a C₁-C₆ polyhydroxyl.

5. (Original) The bifunctional compound of claim 2, wherein, when R' is phenyl or benzyl, said phenyl or benzyl can be substituted with one or more substituents selected from the group consisting of a C₁-C₆ alkyl, a halogen, a C₁-C₆ alkoxy, a C₁-C₆ hydroxyl, and a C₁-C₆ polyhydroxyl.

6. (Original) A compound comprising the bifunctional compound of claim 1 conjugated to a targeting agent.

7. (Original) A compound comprising the bifunctional compound of claim 3 conjugated to a targeting agent.

8. (Original) A compound comprising the bifunctional compound of claim 4 conjugated to a targeting agent.

9. (Original) A compound comprising the bifunctional compound of claim 5 conjugated to a targeting agent.

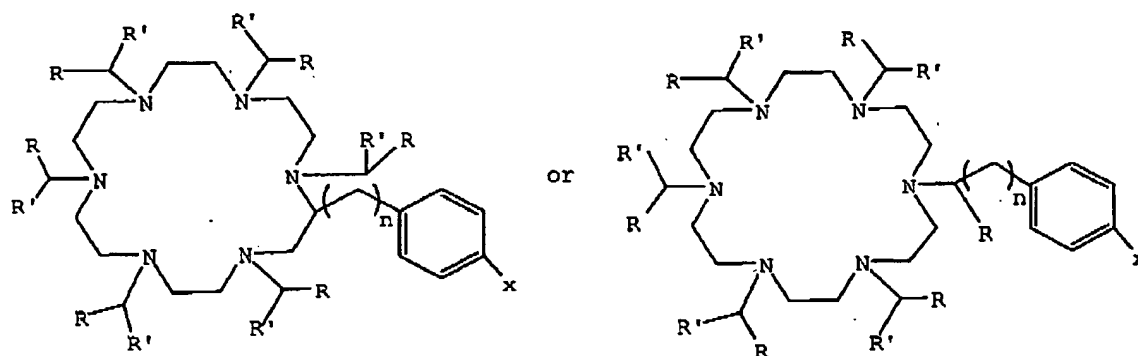
10. (Original) A method of making HEHA, which method comprises:
(i) preparing the free base of the macrocycle 1,4,7,10,13,16-hexaazacyclooctodecane under anhydrous conditions,
(ii) azeotropically removing trace water with benzene,
(iii) N-alkylating the macrocycle to produce the hexaester,

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- (iv) saponifying the hexaester, and
- (v) purifying HEHA.

11. (Original) The method of claim 10, wherein the hexaester is produced by reacting the free base with Na_2CO_3 and tert-butyl bromoacetate in anhydrous CH_3CN .

12. (Original) A method of making a bifunctional HEHA of one of the following formulae:

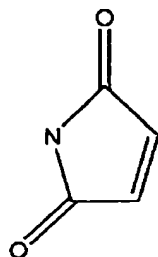


wherein R is selected from the group consisting of CO_2H , CONHR' , P(O)R'OH and P(O)(OR')OH ,

R' is selected from the group consisting of H, a $\text{C}_1\text{-C}_8$ alkyl, phenyl and benzyl, wherein said phenyl or benzyl is substituted or unsubstituted,

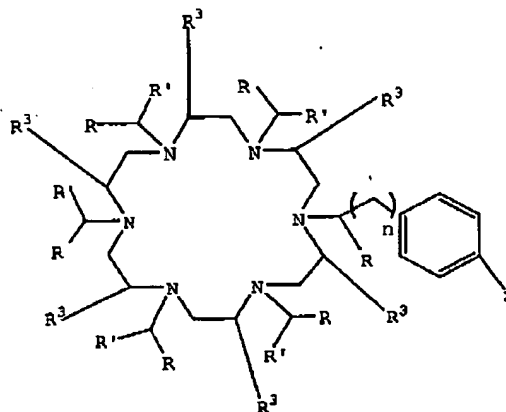
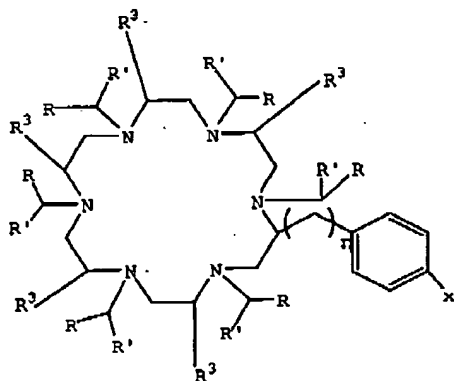
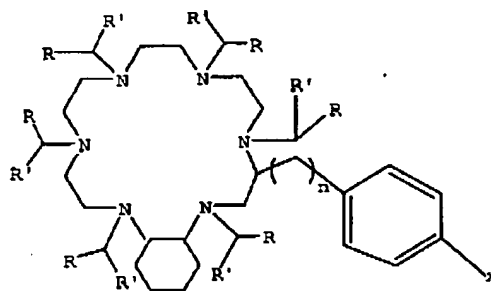
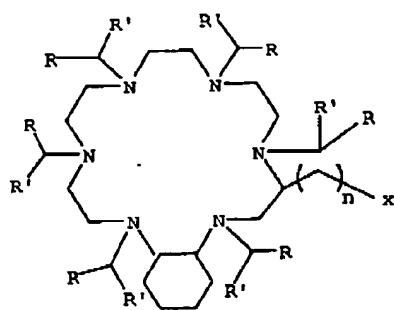
n is 1-6, and

X is selected from the group consisting of NO_2 , NH_2 , NCS, $\text{NHC(O)CH}_2\text{Z}$, in which Z is selected from the group consisting of Cl, Br and I, and

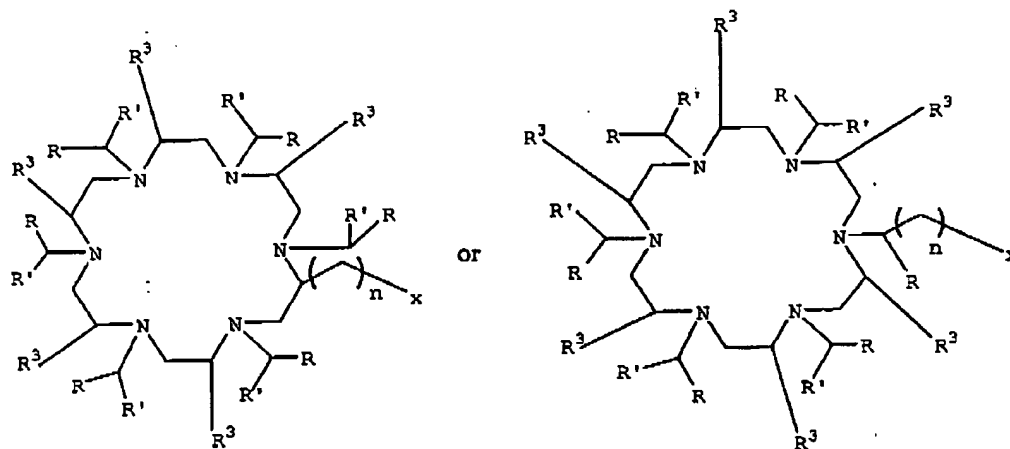


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or one of the following formulae:



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wherein R is selected from the group consisting of CO_2H , CONHR' , $\text{P(O)R}'\text{OH}$ and $\text{P(O)(OR}')\text{OH}$,

R' is selected from the group consisting of H, a $\text{C}_1\text{-C}_8$ alkyl, phenyl and benzyl, wherein said phenyl or benzyl is substituted or unsubstituted,

n is 1-6, and

X is selected from the group consisting of NO_2 , NH_2 , NCS , $\text{NHC(O)CH}_2\text{Z}$, in which Z is selected from the group consisting of Cl, Br and I, and

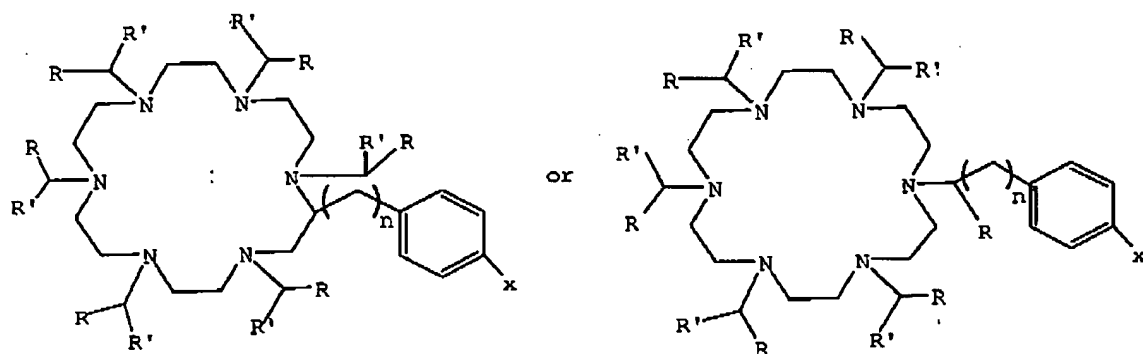
R^3 is selected from the group consisting of H, a $\text{C}_1\text{-C}_6$ alkyl, and benzyl,

which method comprises: (i) preparing a tert-butyloxycarbonyl protected iminodiacetic acid that is condensed with an amino acid ester; (ii) saponifying the resulting diester with a base; (iii) acidifying; (iv) converting to a disuccinimidyl ester; (v) reacting with an N-2-aminoethyl amide of para-nitrophenylalanine; (vi) treating with acid to remove a protecting group; (vii) reducing the amide carbonyl functional groups with diborane; (viii) isolating the resulting macrocyclic polyamine as the protonated salt; (ix) generating the free base; (x) alkylating the free amines to introduce protected R groups; (xi) deprotecting the R groups; (xii) hydrogenating the nitro group to the aniline; and (xiii) converting the aniline to an isothiocyanate, a haloacetamide or a maleimide.

13. (Original) The method of claim 12, which further comprises conjugating the isothiocyanate, the haloacetamide or the maleimide to a targeting agent.

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14. (Original) A method of making a bifunctional HEHA of one of the following formulae:

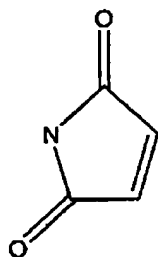


wherein R is selected from the group consisting of CO_2H , CONHR' , $\text{P}(\text{O})\text{R}'\text{OH}$ and $\text{P}(\text{O})(\text{OR}')\text{OH}$,

R' is selected from the group consisting of H, a $\text{C}_1\text{-C}_8$ alkyl, phenyl and benzyl, wherein said phenyl or benzyl is substituted or unsubstituted,

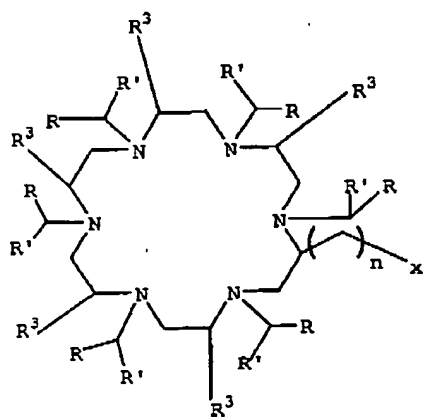
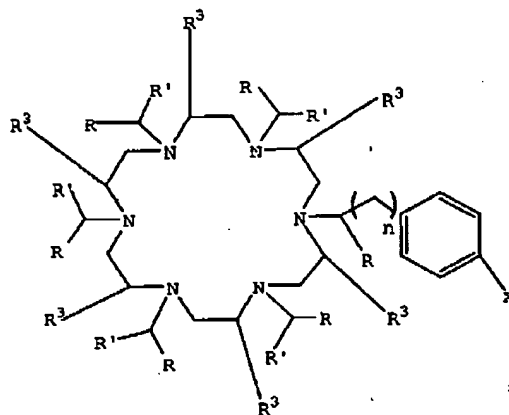
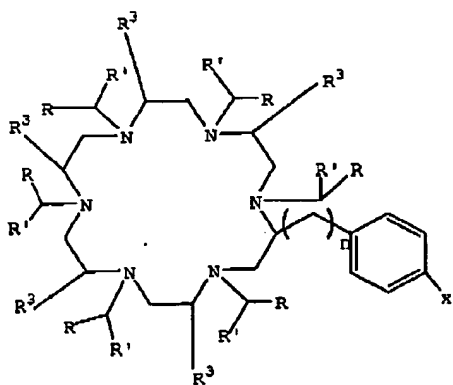
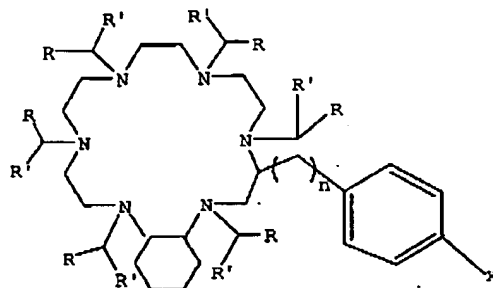
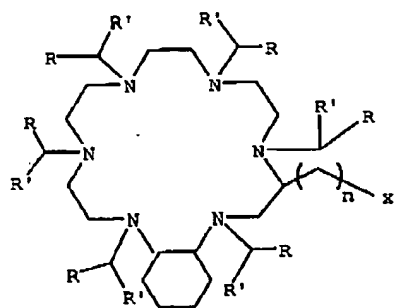
n is 1-6, and

X is selected from the group consisting of NO_2 , NH_2 , NCS , $\text{NHC}(\text{O})\text{CH}_2\text{Z}$, in which Z is selected from the group consisting of Cl, Br and I, and

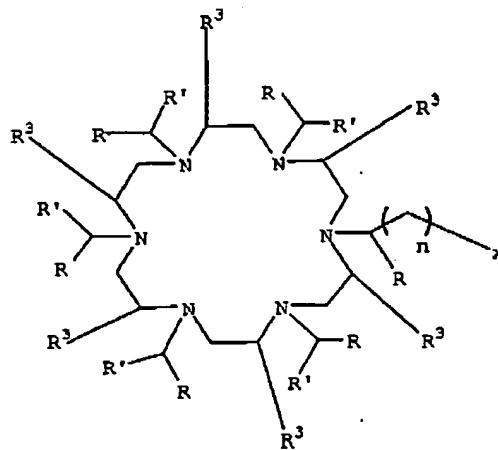


or one of the following formulae:

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or



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wherein R is selected from the group consisting of CO₂H, CONHR', P(O)R'OH and P(O)(OR')OH,

R' is selected from the group consisting of H, a C₁-C₈ alkyl, phenyl and benzyl, wherein said phenyl or benzyl is substituted or unsubstituted,

n is 1-6, and

X is selected from the group consisting of NO₂, NH₂, NCS, NHC(O)CH₂Z, in which Z is selected from the group consisting of Cl, Br and I, and

R³ is selected from the group consisting of H, a C₁-C₆ alkyl, and benzyl, which method comprises:

- (i) preparing a cyclic hexapeptide that comprises one amino acid selected from the group consisting of para-nitrophenylalanine and epsilon-protected lysine;
- (ii) reducing the amide carbonyl functional groups;
- (iii) isolating the resulting macrocyclic polyamine as the protonated salt;
- (iv) generating the free base;
- (v) alkylating the free amines to introduce protected R groups;
- (vi) deprotecting the R groups;
- (vii) hydrogenating the nitro group to the aniline, and
- (viii) converting the aniline to an isothiocyanate, a haloacetamide or a maleimide.

15. (Original) The method of claim 14, which further comprises conjugating the isothiocyanate, the haloacetamide or the maleimide to a targeting agent.

16. (Canceled)

17. (Original) A method of treating cancer, which method comprises administering to a patient having cancer a cancer-treatment effective amount of the compound of claim 6 in which the targeting agent is specific for said cancer.

18. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of ²²⁵Ac-HEHA or a compound of claim 1 and optionally, simultaneously or sequentially,

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peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from ^{225}Ac -HEHA or the compound.

19. (Currently Amended) A method of decontaminating a sample from ^{25}Ac ^{225}Ac , which method comprises contacting said sample with a decontaminating-effective amount of HEHA.

20. (Original) The method of claim 19, wherein said HEHA is attached to a solid support and said sample is a liquid.

21. (Original) A method of decontaminating a person who has been externally contaminated with ^{225}Ac , which method comprises contacting said person with a decontaminating-effective amount of HEHA.

22. (Original) A method of detoxifying a person who has internalized ^{225}Ac , which method comprises administering to said person a detoxifying-effective amount of HEHA.

23. (Original) The bifunctional compound of claim 2, wherein R is CO_2H and R' is H or CH_3 .

24. (Original) A compound comprising the bifunctional compound of claim 2 conjugated to a targeting agent.

25. (Original) A compound comprising the bifunctional compound of claim 23 conjugated to a targeting agent.

26.-30. (Canceled)

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31. (Original) A method of treating cancer, which method comprises administering to a patient having cancer a cancer-treatment effective amount of the compound of claim 24 in which the targeting agent is specific for said cancer.

32. (Original) A method of treating cancer, which method comprises administering to a patient having cancer a cancer-treatment effective amount of the compound of claim 7 in which the targeting agent is specific for said cancer.

33. (Original) A method of treating cancer, which method comprises administering to a patient having cancer a cancer-treatment effective amount of the compound of claim 25 in which the targeting agent is specific for said cancer.

34. (Original) A method of treating cancer, which method comprises administering to a patient having cancer a cancer-treatment effective amount of the compound of claim 8 in which the targeting agent is specific for said cancer.

35. (Original) A method of treating cancer, which method comprises administering to a patient having cancer a cancer-treatment effective amount of the compound of claim 9 in which the targeting agent is specific for said cancer.

36. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 2 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

37. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 3 and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

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38. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 23 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

39. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 6 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

40. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 24 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

41. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 7 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

42. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 25 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

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43. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 8 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.

44. (Original) A method of treating a solid tumor, which method comprises intratumorally administering to a patient having a tumor a tumor-treatment effective amount of a compound of claim 9 in which the targeting agent is specific for the tumor and optionally, simultaneously or sequentially, peritumorally administering to the patient HEHA in an amount effective to chelate any radioactive decay products from the compound.